Particle-based methods for Tissue Engineering

Modeling mechanical interactions in 3D cell cultures

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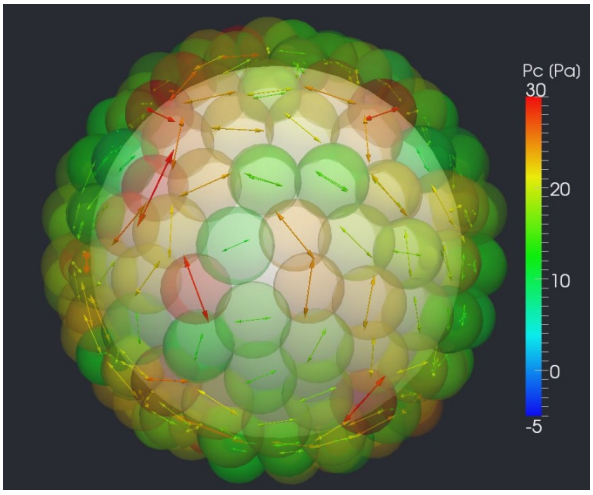
In order to manufacture three-dimensional cell aggregates that can be used in Tissue Engineering applications, cell culture systems and scaffolds should be designed that offer optimal growth conditions for the cells as well as control of cell fate. These systems facilitate a structural organization of 3D cell aggregates, providing not only appropriate spatial gradients of growth factors and access to oxygen and nutrients, but also establishing a suitable mechanical environment for the cells. This mechanical micro-environment is determined by external factors, such as the properties of the medium flow, or the characteristics of the biomaterials to which the cells adhere, as well as by the behaviour of the cells themselves. By growing, migrating or contracting, cells actively modify their mechanical microenvironment. Modelling techniques help unravelling how the design of cell culture systems, combined with cell biological behaviour, influences the mechanical properties of the cells' micro-environment.



Compressive stress and direction of stress at confluency in microcarrier aggregate

We present a framework for lattice-free, particle-based simulations which emphasizes cell-cell and cell-substrate mechanical interactions. An individual-cell based model of cell proliferation on non-porous spherical microcarriers has been implemented. The model describes cell proliferation from a purely morphological point of view, includes cell motility and Brownian motion, and calculates contact forces from a JKR potential. Cells are randomly seeded on the surface of a dense microcarrier and grow until confluency. The simulations show that a large heterogeneity in (mainly compressive) mechanical stress can be expected when the cells reach confluency. Both cell-microcarrier adhesion energy (influenced by the carrier's coating) as well as the bead size have an effect on the compressive stresses on the cells. In addition, simulations of growth on a flat surface (e.g. a petri dish) have been performed. Also in this case, mechanical heterogeneity is observed upon confluency, and depending on the growth properties interesting spatial patterns in mechanical stress arise.

Finally, we present a detailed deformable cell model with the aim of improving shape representation of cells attached to a substrate. This model is based on a red blood cell model published previously, combined with a simple representation of the cytoskeleton to capture the cells' immediate elastic response to compression. Using this model, we predict local compressive normal forces at confluency in the order of 100 Pa and an overall cortical tension of around 5 $\mu J/m^2$.